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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,530	03/17/2004	Jonathan Bingham	37087-8005.US01	3519
79975	7590	05/26/2009		
King & Spalding LLP P.O. Box 889 Belmont, CA 94002-0889			EXAMINER RIGGS II, LARRY D	
			ART UNIT 1631	PAPER NUMBER
			MAIL DATE 05/26/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/802,530

Applicant(s)

BINGHAM ET AL.

Examiner

LARRY D. RIGGS II

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/SE/US)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's amendments filed 02 March 2009 are acknowledged and entered.

Status of Claims

Claims 1-14 are cancelled. Claims 15-21 are currently pending and under consideration.

Withdrawn Rejections/Objections

The rejection of claims 15-21 under 35 U.S.C. 112, second paragraph, in the Office action mailed 01 October 2008 is withdrawn in view of the amendments filed 02 March 2009.

The rejection of claims 15-21 under 35 U.S.C. 103(a) over Lorraine et al., in the Office action mailed 01 October 2008 is withdrawn in view of the amendments filed 02 March 2009.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

This rejection is maintained and reiterated from the previous office action, mailed 01 October 2008.

Claims 15-21 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims are drawn a method in a computer system for displaying a graphical representation of expression levels of a plurality of splice variants of a gene in one or more samples. The instant claims are drawn the abstract process steps of identifying modules for each splice variant of the gene, applying a first mathematical function to the length of a first module, applying a second mathematical function to the length of a second module, determining a relative expression level for each of the plurality of splice variants by applying a mathematical algorithm to expression level data, and displaying a graphical representation of the splice variants on an output device linked to a suitably programmed computer.

The Supreme Court has enunciated a definitive test to determine whether a process claim is tailored narrowly enough to encompass only a particular application of a fundamental principle rather than to pre-empt the principle itself. A claimed process is surely patent-eligible under §101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing. See *Benson*, 409 U.S. at 70; *Diehr*, 450 U.S. at 192; see also *Flook*, 437 U.S. at 589 n.9; *Cochrane v. Deener*, 94 U.S. 780, 788 (1876).

In the instant method claims 15-21, there is no physical transformation by the claimed invention because identifying modules, applying mathematical functions, determining a relative expression level with an algorithm and displaying a graphical representation are not physical transformations. Displaying a representation on an output device is not a physical transformation of data.

Therefore the Examiner must determine if the instant claims have a tie to a particular machine or apparatus. Instant claims 15-21 do not recite any limitation that ties the recited abstract process to any particular machine or apparatus. Further, claims 15-21 only recite displaying a graphical representation...on an output device linked to a suitably programmed computer, last line of the instant claim 15. Neither the output device nor the suitably programmed computer is a particular machine or apparatus. The output device is a general purpose display device. Likewise, the suitably programmed computer is only post-solution activity that reads on a general apparatus that would preempt the abstract process. Similarly, "a method in a computer system..." in line 1 of the instant claim 15, is just a method and the "computer system" is considered inconsequential.

Further, displaying said representation is an insignificant post-solution activity. Nominal or token recitations will not suffice, E.g. displaying, inputting, obtaining, See Ex parte Langemyr (May 28, 2008). Applicants are cautioned against introduction of new matter in an amendment.

For these reasons, claims 15-21 are considered non-statutory subject matter.

Response to Arguments

Applicant's arguments filed 02 March 2009 have been fully considered but they are not persuasive.

Applicants argue that the physical step of nucleic acid hybridization is subsequently "transformed" into expression data, which is then use din an algorithm, satisfying the legal standards for patentability under 35 U.S.C. §101. Likewise, the instant claim 15, is amended to recite an output device linked to a suitably programmed computer.

Applicant's arguments are not persuasive.

Applicants obtain relative expression data from probes with an algorithm, and then display the data that is displayed corresponding to the respective exon of the splice variant. This is nothing more than obtaining and correlating data. This is not transformation of a particular article into a different state or thing. See *Benson*, 409 U.S. at 70; *Diehr*, 450 U.S. at 192; see also *Flook*, 437 U.S. at 589 n.9; *Cochrane v. Deener*, 94 U.S. 780, 788 (1876). The court has frequently stated that adding a data-gathering step to an algorithm is insufficient to convert that algorithm into a patent-eligible process. E.g., *Grams*, 888 F.2d at 840 (step of "deriv[ing] data for the algorithm will not render the claim statutory"); *Meyer*, 688 F.2d at 794 ("[data-gathering] step[s] cannot make an otherwise nonstatutory claim statutory"). The display of a representation on an output device via a suitably programmed computer do not suffice as a method linked to a particular machine or apparatus as discussed above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Loraine et al. (US 2004/0049354) in view of Rossignol et al. (Genomics, 2000, 70, 211-222).

The claims are drawn a method in a computer system for displaying a graphical representation of expression levels of a plurality of splice variants of a

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gene in one or more samples, each of the plurality of splice variants of the gene having modules the method comprising:

identifying modules for each splice variant of the gene, wherein each module represents an exon or an intron of a splice variant of a gene and has a length,

applying a first mathematical function to the length of a first module of a first splice variant to obtain a scaled length for the first module of a first splice variant for graphical representation,

applying a second, different, mathematical function to the length of a second module of a first splice variant to obtain a scaled length for the second module for graphical representation,

determining a relative expression level for each of the plurality of splice variants by applying a mathematical algorithm to expression level data obtained using exon-exon junction indicator polynucleotides that selectively hybridize to exon-exon junctions of the plurality of splice variants, and

displaying a graphical representation wherein the modules of the splice variants are aligned to each other, wherein the representation indicates the relative expression levels of each of the plurality of splice variants of the gene and wherein the scaled length of the first module and the scaled length of the second module are displayed simultaneously on an output device linked to a suitably programmed computer.

Regarding claim 15, Loraine et al. shows modules, (e.g. Figure 3 of applicant's disclosure) of multiple splice variants with various lengths, (see

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paragraph 139; Figure 12); scaling the length of the modules of splice variants with a variety of scales that may vary in units and magnitude including linear, logarithmic and other types of scales, (see paragraph 137); applying a hybridization data to a model-fitting algorithm, wherein data may be obtained from exon-exon junction probes, i.e. data obtained from hybridizing exon-exon junction probes to splice variants, (see paragraphs 88, 89 and 113); and displaying a graphical representation of modules of splice variants, wherein the representation indicates relative expression levels of the splice variants (see paragraphs 5, 140, 141 and 144; Figure 12).

While Loraine et al. shows different mathematical scaling to lengths of the modules of splice variants, (paragraph 137), Loraine et al. only displays modules of exons or introns simultaneously in one scale. Loraine does not show different scaled lengths of modules (exon or intron) displayed simultaneously.

Rossignol et al. shows introns and exons displayed simultaneously with different scaled lengths, (Figure 1).

Regarding claim 16, Loraine et al. shows non-overlapping exons and modules (see paragraph 144; Figure 12, 1210).

Regarding claim 17, the specification in paragraph 38, provides that the invention may display trimmed or extended exon in one module, while the remainder of the exon is another module. This is interpreted to mean that a partial exon may be displayed. Loraine et al. shows displaying modules of exons, introns or partial exons, (see paragraph 144).

Regarding claim 18, Loraine et al. shows exons and modules are constitutive, (See Figure 12, top two splice variants of 1210).

Regarding claim 19, Loraine et al. shows exons and modules are non-constitutive, (See Figure 12, comparing top two splice variants of 1210 with third splice variant of 1210, also referred in the figure 12 as 1211, selected splice variant).

Regarding claims 20 and 21, Loraine et al. shows scaling the length of the modules and exons of splice variants with a variety of scales that may vary in units and magnitude including linear, logarithmic and other types of scales, (see paragraph 137). This is interpreted to mean that to change scales by linear units or logarithmically, means to apply a linear or logarithmic function to the measured units of the current scale, respectively, (see paragraphs 137-138; Figure 12).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of analysis of alternative splice variants by Loraine et al. by simultaneously displaying different modules of splice variants on different scales as in Rossignol et al. because Loraine et al. shows "it will be understood that many other graphical arrangements or devices known to those skill in the art may be used to distinguish splice variants and/or distinguish exons belonging to one or more splice variants", (paragraph 137) and one having ordinary skill in the art would understand that exons and introns usually vary greatly in size and it would be obvious to display exons and introns of a splice variant simultaneously would require an intron to be at a different scale, e.g. logarithmic scale, with respect to an intron within the same splice variant.

Therefore, one of ordinary skill in the art would recognize the claimed process as a combination of routine applications that are well known the art that and produce no more than expected results.

Response to Arguments

Applicant's arguments filed 02 March 2009 have been fully considered but they are not persuasive.

Applicants argue that Loraine et al. does not show or suggest two different mathematical functions to two different modules in a single splice variant. Loraine et al. does not teach representation of relative expression levels of individual splice variants. Loraine et al. does not disclose application of a mathematical algorithm to expression level data to determine the relative expression levels of each of a plurality of splice variants.

Loraine et al. shows that each alternative splice variant could have different expression patterns and function, (paragraph 87). Loraine et al. shows that those of ordinary skill in the relevant art that numerous alternative formats, both textual and graphical may be used in other implementations that shown in Figure 12. (paragraph 133), that a variety of scales that may vary in units and magnitude including linear, logarithm, and other types of scales and the alternative splice variant an/or gene aligned in this manner may have been selected by a user in accordance with any of the techniques noted therein wherein variants and/or their exons may be color-coded, identified by differently shaped object, arranged differently and so-on, (paragraph 137). See above.

Loraine et al. shows the measure of abundance could include the relative expression level of each alternative splice variant, the frequency of exon usage in all alternative splice variant, or other user-selected measure, i.e. the height of exon bar (1265) of Figure 12, may correspond, as one of the examples noted above, to the frequency with an exon or partial exon, occurs in the alternative splice transcripts, or various bar heights may occur within each exon and between different exons, (paragraph 144). Loraine et al. shows that each alternative splice variant could have different expression patterns and function, (paragraph 87).

Loraine et al. shows applying hybridization data to a model-fitting algorithm, wherein data may be obtained from exon-exon junction probes, i.e. data obtained from hybridizing exon-exon junction probes to splice variants, (see paragraphs 88, 89 and 113).

Loraine et al. in view of Rossignol et al. meets all the limitations of the instant invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LDR/
Larry Riggs
Examiner, Art Unit 1631

/ERIC S. DEJONG/
Primary Examiner, Art Unit 1631